REMARKS

Status of the Claims

Claims 1 to 9 and 21 to 27 were pending. Claim 1 has been amended to make explicit that the responsive element comprises a transcription activation element. Accordingly, claim 2 has been canceled without prejudice or disclaimer and claim 3 has been amended to depend from claim 1, rather than canceled claim 2. Thus, claims 1 to 9 and 21-27 are pending as shown above. Applicants note with appreciation that claims 24-26 would be allowable if rewritten in independent form.

Rejections Withdrawn

Applicants note with appreciation that the obviousness-type double patenting rejection and the rejection of claim 22 under 35 U.S.C. § 112, first paragraph have been withdrawn.

Rejection Under 35 U.S.C. §102(b)

In the Advisory Action, it was indicated that amended claims 1-9, 22, 23 and 27 would be rejected under 35 U.S.C. §102(b) as allegedly obvious over Karube & Nakanishi (1994) *Current Opin Biotech* 5:54-59 (hereinafter "Karube") in light of Sleight. (Advisory Action, page 5). It was maintained that Karube teaches cells comprising biodetectors for the detection and analysis of specific substrates and that Sleight teaches the processes and components involved in signal transduction and illustrates that the biodetector disclosed by Karube inherently possesses the properties of the claimed biodetectors. (Advisory Action, page 5).

Applicants traverse the rejection and supporting remarks.

In order to be an anticipatory reference, the reference cited by the Office must disclose each and every element of the claims, including each and every functional or biological limitation. *See, e.g., Hybritech v. Monoclonal Antibodies,* 231 USPQ 81 (Fed. Cir. 1986); M.P.E.P § 2173.05(g) Functional Limitations, Eighth Edition. Moreover, the single source must disclose all of the claimed elements arranged as in the claims. *See, e.g., Richardson v. Suzuki Motor Co.,* 9 USPQ2d 1913 (Fed. Cir. 1989). Simply put, the law requires identity as between the prior art disclosure and the invention. *See, e.g., Kalman v. Kimberly-Clark Corp.* 218 USPQ 781 (Fed. Cir. 1983), *cert. denied,* 484 US 1007 (1988). Thus, the references must teach all elements of the claims, explicitly or inherently, including functional limitations such as biological function.

The pending claims are directed to biodetectors in which a ligand must specifically bind to an extracellular moiety that in turn activates the intracellular moiety of the signal-converting element. The activated intracellular moiety then converts a transducer from an inactive to active form and, finally, the activated transducer activates a responsive element comprising a transcription activation element to produce a detectable signal.

In contrast, Karube fails to disclose biodetectors in which a transducer activates a responsive element comprising a transcription control element. Rather, as noted in the Advisory Action, Karube, on page 54, right column, 3rd full paragraph, describes that transducers are "used to convert the biochemical signal into an electronic signal that can be suitably processed and outputted." Clearly, Karube does not teach transducers that activate a responsive element comprising a transcription control element, as set forth in the pending claims. Rather, as discussed in further detail below, when the responsive element comprises a transcriptional control element, Karube teaches biosensors lacking a transducer entirely and/or in which a transducer decreases luciferase activity in naturally-occurring photobacteria.

Specifically, it is clear that in the specific context of photo-biosensors, Karube fails to teach biodetectors in which an activated transducer in turn actives a responsive element, as claimed. The systems discussed on page 55 left column to page 56, left column, 1st full paragraph of Karube plainly evaluate the decrease (if any) in luminescence (see, e.g., Karube, page 56, 1st full paragraph, emphasis added):

> Engineering of a membrane mutant of this luminescent strain of *E. coli* permitted a considerable increase in sensitivity to toxic substances compared with the wild type. Both pesticides and herbicides were detectable by the **decrease** in luminescence.

Thus, the photobacterial biosensors described in these passages of Karube cannot anticipate the pending claims, all of which require activation of a responsive element by an activated transducer.

Moreover, the other systems in Karube that actually involve activation of luciferase in genetically engineered cells, do **not** describe or demonstrate activation via an activated transducer, as claimed. Rather, the "ligand" (*i.e.*, aluminum or mercury) itself stimulates luciferase activity directly (see, page 56, 2nd and 3rd full paragraphs, emphasis added):

> **Aluminum stimulates luciferase enzyme activity** when the *luxAB* genes are located in the *xyl* operon [citations omitted].

> The plasmid was constructed such that the expression of *lux* genes was under the control of the *mer* regulatory gene and promoter, which activate the expression of the *lux* genes in the presence of mercury. **The light can be readily detected and quantified, resulting in a biosensor for the detection of mercury** [citation omitted].

Simply put, Karube doesn't teach biodetectors having a transducer, which, in its activated form, activates a responsive element. Indeed, the direct assays described in Karube are totally unlike the claimed biodetectors, which all use signal-transduction mechanisms. As described throughout the specification as filed, signal transduction assays have much wider applicability and scope than Karube's direct assays.

With regard to the allegation in the Advisory Action that diphtheria toxin specifically binds to a heparin-binding epidermal growth factor precursor, Applicants note the following. First and foremost, not only does Karube not mention diphtheria, but, for the reasons noted above, also fails to disclose a biodetector in which a diphtheria toxin would activate a transducers which would in turn activate a responsive element. Second, Karube clearly indicates that the exemplary photobacterial systems "demonstrate the utility of photomicrobial sensors in a number of environmental monitoring applications." (Karube, page 56, left column, 4th full paragraph). Diphtheria is not typically considered an environmental toxin. Therefore, Karube does not disclose the subject matter of the pending claims.

Finally, because Karube is entirely unrelated to signal transduction pathways and, instead, relates only to direct assays, the disclosure cannot be properly viewed in light of Sleight, which relates entirely to signal transduction pathways, all of which are characterized by the fact that the ligand does not itself enter the cell.

Thus, it is plain that a biodetectors as claimed, are not disclosed in Karube, either alone or in light of general references regarding signal transduction pathways.

CONCLUSION

Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

If the Examiner notes any further matters that the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

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Respectfully submitted,

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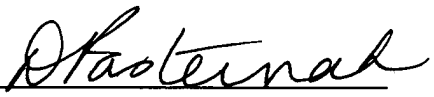
By: 
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